

Claims

What is claimed is:

1. A pharmaceutical formulation for extended release of buprenorphine from
5 microspheres, said formulation made by steps comprising:

admixing PLGA having a first specific viscosity with PLGA having a
second specific viscosity to form a PLGA mixture;

admixing the PLGA mixture with a halogenated organic solvent to form a
PLGA-halogenated organic solvent mixture;
10 admixing the PLGA-halogenated organic solvent mixture with
buprenorphine to form a buprenorphine-PLGA-halogenated organic
solvent mixture;

admixing a buffered aqueous solution of PVA with the buprenorphine-
PLGA-halogenated organic solvent mixture to form an emulsion
15 comprising microspheres, said microspheres comprising buprenorphine;
recovering at least one of said microspheres from the emulsion.
2. A pharmaceutical formulation according to claim 1, wherein the buprenorphine
with which the PLGA-halogenated organic solvent mixture is admixed comprises
20 buprenorphine free base.

3. A pharmaceutical formulation according to claim 2, wherein the buprenorphine with which the PLGA-halogenated organic solvent mixture is admixed consists essentially of buprenorphine free base.
- 5 4. A pharmaceutical formulation according to claim 1, wherein the buffered aqueous solution of PVA comprises phosphate.
5. A pharmaceutical formulation according to claim 1, wherein the concentration of PVA in the buffered aqueous solution of PVA is about 0.1% (w/v).
- 10 6. A pharmaceutical formulation according to claim 1, wherein the pH of the buffered aqueous solution of PVA is between about 6.8 and about 8.0.
7. A pharmaceutical formulation according to claim 6, wherein the pH of the
15 buffered aqueous solution of PVA is about 7.4.
8. A pharmaceutical formulation according to claim 4, wherein the buffered aqueous solution of PVA comprises at least one of the group consisting of sodium phosphate and potassium phosphate.
- 20 9. A pharmaceutical formulation according to claim 1, wherein the first specific viscosity is between about 0.01 and about 0.31 dL/g and the second specific viscosity is between about 0.40 and 0.88 dL/g.

10. A pharmaceutical formulation according to claim 9, wherein the first specific viscosity is between about 0.12 and about 0.20 dL/g and the second specific viscosity is between about 0.48 and 0.80 dL/g.

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11. A pharmaceutical formulation according to claim 10, wherein the first specific viscosity is between about 0.14 and about 0.18 dL/g and the second specific viscosity is between about 0.56 and 0.72 dL/g.

10 12. A pharmaceutical formulation according to claim 11, wherein the first specific viscosity is about 0.16 dL/g and the second specific viscosity is about 0.64 dL/g.

13. A pharmaceutical formulation according to claim 1, wherein the halogenated organic solvent comprises dichloromethane.

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14. A pharmaceutical formulation according to claim 13, wherein the halogenated organic solvent consists essentially of dichloromethane.

15. A pharmaceutical formulation according to claim 1, wherein the admixing of the
20 buffered aqueous solution of PVA with the buprenorphine-PLGA-halogenated organic solvent mixture comprises sonication.

16. A formulation according to claim 1, wherein the recovering comprises at least one of the group consisting of sedimentation and lyophilization.
17. A process for making a pharmaceutical formulation for extended release of
5 buprenorphine from microspheres, said process comprising:
- admixing PLGA having a first specific viscosity with PLGA having a second specific viscosity to form a PLGA mixture;
 - admixing the PLGA mixture with a halogenated organic solvent to form a PLGA-halogenated organic solvent mixture;
 - 10 admixing the PLGA-halogenated organic solvent mixture with buprenorphine to form a buprenorphine-PLGA-halogenated organic solvent mixture;
 - admixing a buffered aqueous solution of PVA with the buprenorphine-PLGA-halogenated organic solvent mixture to form an emulsion
 - 15 comprising microspheres, said microspheres comprising buprenorphine;
 - recovering at least one of said microspheres from the emulsion.
18. A process according to claim 17, wherein the buffered aqueous solution of PVA comprises at least one of the group consisting of sodium phosphate and potassium
20 phosphate.
19. A process according to claim 17, wherein the buprenorphine consists essentially of buprenorphine free base.

20. A method of treating a mammal in which treatment with buprenorphine is indicated, said method comprising the step of administering to the mammal a pharmaceutically effective quantity of buprenorphine-containing microspheres prepared
- 5 by a process comprising:
- admixing PLGA having a first specific viscosity with PLGA having a second specific viscosity to form a PLGA mixture;
 - admixing the PLGA mixture with a halogenated organic solvent to form a PLGA-halogenated organic solvent mixture;
 - 10 admixing the PLGA-halogenated organic solvent mixture with buprenorphine to form a buprenorphine-PLGA-halogenated organic solvent mixture;
 - admixing a buffered aqueous solution of PVA with the buprenorphine-PLGA-halogenated organic solvent mixture to form an emulsion
 - 15 comprising microspheres, said microspheres comprising buprenorphine;
 - recovering at least one of said microspheres from the emulsion.